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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/943,664	08/30/2001	Kevin P. Baker	P2548P1C8	2448

7590 09/24/2003

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	17

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/943,664	BAKER ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 22-34 are pending in the instant application. Claims 22-26 have been amended as requested by Applicant in Paper Number 16, filed June 26, 2003.

All claims are currently under examination.

Objection to Specification

2. The objections to the specification are withdrawn in view of Applicants' amendment.

Withdrawn Objections and Rejections

3. Any objection or rejection of record which is not expressly repeated in this action has been withdrawn.

Priority Determination

35 U.S.C. § 120 states that:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

35 U.S.C. § 119(e) states that:

> An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

4. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 or § 119(e) from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention. Because the instant application does not meet the requirements of 35 U.S.C. § 112, first paragraph, for those reasons given above, the prior applications also do not meet those requirements and, therefore, are unavailable under 35 U.S.C. § 120 or § 119(e). Since this application is a continuation of PCT/US99/28301, filed Dec. 1, 1999, the effective priority date of the instant application is considered to be the filing date of that application, because the claimed invention is not supported by either a specific and substantial utility or a well established utility.

New Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 22-27, 31, 33 and 34 are rejected under 35 U.S.C. 102(e) as being anticipated by Holtzman et al., US Patent Application Publication US20020028508, effective filing date, April 23, 1998 (09/065,661).

Claims 22-27, 31, 33 and 34 encompass a polypeptide having at least 80%, 85%, 90% or 95% sequence identity to the polypeptide of SEQ ID NO: 50, or 99% or 100% identity to the amino acid sequence of the extracellular domain of SEQ ID NO: 50 lacking its associated signal

peptide, and chimeric polypeptide fused to a heterologous polypeptide, wherein the heterologous polypeptide is an epitope tag or an Fc region of an immunoglobulin.

Holtzman et al. disclose a protein (SEQ ID NO: 2) that is 96.8% identical to the protein of SEQ ID NO: 50 of the instant invention (see attached sequence alignments). The instant application identifies the signal sequence as amino acids 1-26 and the extracellular domain as amino acids 27-109 of SEQ ID NO: 50, the extracellular domain. The protein of Holtzman is identical to the extracellular domain, amino acids 27-109, of SEQ ID NO: 50. Holtzman et al. also teach chimeric proteins, wherein the heterologous polypeptide is an epitope tag or an immunoglobulin (paragraph 0418, 0221 and 0224). Therefore, Holtzman et al. anticipates the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 22-27, 31, 33 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-27, 31, 33 and 34 are indefinite because claims 22-27, 30 and 31 encompass a polypeptide comprising the extracellular domain of the protein of SEQ ID NO: 50. The recitation of "the extracellular domain"..." lacking its associated signal sequence" (claim 22, part (d), for example) is indefinite as a signal sequence is not generally considered to be part of

an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell. The other claims are rejected for depending from claim 22.

Response to Amendment

7. The declaration under 37 CFR 1.132 filed June 26, 2003 is insufficient to overcome the rejection of claims 22-34 based upon lack of utility under 35 U.S.C. § 101 as set forth in the last Office action because: the declaration has overcome the lack of utility for the nucleic acid of SEQ ID NO: 49, because the nucleic acid molecule of SEQ ID NO: 49 would have utility, and would be enabled, as being useful as a probe to diagnose certain cancers. However, the claims are directed to polypeptides, not DNA, and the rejection is maintained, for the reasons below under 35 U.S.C. § 101.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 22-34 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The basis for these rejections is set forth at pp. 3-6 of the previous Office Action (Paper No. 15, 24 March 2003).

Applicant's arguments (pp. 9-11, Paper No. 16, 26 June 2003) have been fully considered but are not found to be persuasive for the following reasons.

Applicant refers to the attached Goddard declaration (filed under 37 CFR 1.132) as providing evidence that one skilled in the art accepts gene amplification data as an indicator of cancerous tissue. The evidence presented in the declaration has been carefully considered. The examiner concedes that the declaration successfully addresses the concerns raised in the previous Office Action regarding the significance of a difference of 1 or 2 PCR cycles, and that proper controls for aneuploidy were used. Thus the nucleic acid molecule of SEQ ID NO: 49 would have utility, and would be enabled, as being useful as a probe to diagnose certain cancers.

However, the claims are directed to polypeptides, not DNA. Applicant argues that the proteins encoded by the DNA and antibodies directed against the protein would be expected to have utility as cancer diagnostic agents. This argument is not found to be persuasive, and the Goddard declaration under 37 CFR 1.132 filed 26 June 2003 is insufficient to overcome the rejection of claims 22-34 based upon 35 U.S.C. §§ 101 and 112, first paragraph, as set forth in the last Office action for the following reasons.

The data in the specification (and reviewed in the declaration) show that gene copy number is increased in certain tumor tissue samples. However, it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased protein expression, such that the antibodies would be useful diagnostically or as a target for cancer drug development. For example, Pennica et al. (1998, PNAS USA 95:14717-14722; Exhibit A of the declaration) disclose that,

> "An analysis of *WISP-1* gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP-3* RNA was seen in the absence of DNA amplification. In contrast, *WISP-2* DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See p. 14722, second paragraph of left-hand column; pp. 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors". Furthermore, an increase in mRNA expression does not necessarily result in increased protein expression. See Haynes et al. (1998, Electrophoresis 19:1862-1871), who studied more than 80 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between protein and transcript level. For some genes, equivalent mRNA levels translated into protein abundances which varied more than 50-fold. Haynes et al. concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript) p. 1863, second paragraph, and Figure 1).

Therefore, the claimed invention, directed to polypeptides, remains rejected under 35 U.S.C. § 101 for lack of utility and 35 U.S.C. § 112, first paragraph, for lack of enablement.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9.1 Claims 22-34 also remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if the specification were enabling of how to use the PRO347 polypeptide, enablement would not be found commensurate in scope with the claims. Even if there were a patentable use for the protein of SEQ ID NO: 50, variants of 80-99% identity would not be enabled because the specification has not taught one of ordinary skill

in the art how to use them or fragments thereof.

Applicants have demonstrated that the nucleic acids can be used as a diagnostic for a tumor in a tissue, because they are amplified in certain tumors. However, claims 22-34 encompass polypeptides. Applicants have amended the claims to recite the limitation "wherein said polypeptide is overexpressed in lung and colon tumors", and on pages 14-15 assert that such variant and fragment polypeptides would have the same diagnostic utility as the wild-type PRO347 polypeptide, in that such variant and fragments of PRO347 would have the same or at least similar utility to full length polypeptides in detecting, monitoring or preparing treatments for various cancers. Applicants also cite *in re Wands* and assert that a considerable amount of experimentation is permissible, if it is routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

Applicants' arguments have been fully considered but are not deemed persuasive. The data in the specification (and reviewed in the declaration) show that gene copy number is increased in certain tumor tissue samples. However, as discussed above, it is not predictable that the PRO347 polypeptide is overexpressed in any tumor cell in which the encoding nucleic acid is amplified, and the rejection is maintained.

9.2 Claims 22-26, 33 and 34 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants traverse the rejection and have amended the claims to recite the limitation "wherein said polypeptide is overexpressed in lung and colon tumors", and assert on pages 13-15

of the response that as amended, the claims satisfy the written description requirement. Applicants submits that the present application discloses a combination of the elements required for an adequate written description (paragraph bridging pages 13-14 of the response), and that the claims have been amended such that the claimed variant and fragment polypeptides are required to have a sufficient sequence identity with the wild type PRO347, in addition to the functional limitation of a polypeptide that is overexpressed in lung and colon tumors.

Applicants' arguments have been fully considered but are not deemed persuasive. As discussed above, amplification of a nucleic acid does not necessarily result in an increase of the encoded polypeptide, and therefore the functional recitation is not considered adequate to overcome the written description requirement, and the rejection is maintained.

Rejections over Prior Art
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Because this application is a continuation of PCT/US99/28301, filed Dec. 1, 1999, it has been determined that this is the effective priority date for the instant application.

10. Claims 22-34 remain rejected under 35 U.S.C. 102(a) (formerly 102(b)) as being anticipated by Botstein et al., WO 99/35170, July 15, 1999, claims 22-27, 31, 33 and 34 remain rejected under 35 U.S.C. 102(a) (formerly 102(b)) as being anticipated by Holtzman, WO 99/54343, Oct. 28, 1999.

Applicants traverse the rejections and assert that the proper priority date of the instant application is Dec. 22, 1998, before the Botstein et al. and Hotlzman were published, and Applicant also notes that Botstein et al. is a Genentech application, filed the same day as provisional application 60/113,296, to which Applicant states it is entitled to priority, and the priority application has the same specification as the reference cited by the Examiner.

Applicants' arguments have been fully considered but are not deemed persuasive. Although Botstein et al. is a Genentech application and was filed the same day as provisional 60/113,296, the effective priority date for the instant application is Dec. 1, 1999, because Applicants have not overcome the utility rejection, and the Botstein et al. reference has a different inventive entity and does not claim priority to the same applications. Holtzman also was published prior to the priority date for the instant application. Therefore, the rejections are maintained.

It is believed that all pertinent arguments have been answered.

Conclusion

11. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner

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